Amendment

In the Claims

1. (currently amended) A conjugate for use in targeting a drug to a tissue,

~~wherein the tissue overexpresses a digestive enzyme,~~ the conjugate comprising: a polymeric carrier; a drug molecule; and ~~a linker~~ an enzyme cleavage site that is cleaved by a serine protease or matrix metalloproteinase, that includes a first end and a second end, and is selected from the group consisting of HSSKLQ (SEQ ID NO:2), SS(Y/F)YS(G/S) (SEQ ID NO:3), Q/E)(R/K/H)RLXY (SEQ ID NO:4), PFT, KKSPGRVVGGSVAAH (SEQ ID NO:5), GPR, GPK, AP, RPPGFSPFR (SEQ ID NO:6), YEEEEI (SEQ ID NO:7), SNFDDY (SEQ ID NO:8), WMDF (SEQ ID NO:9), PLPL (SEQ ID NO:10), RR, FR, AND FR;

wherein the polymeric carrier is associated with the first end of the ~~linker~~ enzyme cleavage site and the drug is associated with the second end of the ~~linker~~ enzyme cleavage site,

~~wherein the polymeric carrier-conjugate is greater than about 6 nm in size,~~

~~wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and~~

~~wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases~~ and the polymeric carrier has a molecular weight of 50,000 or more or is greater than 6 nm in size.

2. (cancelled)

3. (original) The conjugate of claim 1, wherein the polymeric carrier is hydrophilic, biocompatible and biodegradable.

4. (cancelled).

5. (original) The conjugate of claim 1, wherein the drug is a small molecule drug.

6. (original) The conjugate of claim 1, wherein the drug is a biomolecular drug.

7-10. (canceled).

11. (original) A pharmaceutical composition comprising a pharmaceutically acceptable excipient and an effective amount of the conjugate of claim 1.

12. (currently amended) A method of preparing a conjugate ~~for use in targeting a drug to a tissue, wherein the tissue overexpresses a digestive enzyme~~, the method comprising:

providing a polymer carrier; providing a drug molecule; providing ~~a linker~~ an enzyme cleavage site that is cleaved by a serine protease or matrix metalloproteinase that includes at least a first end and a second end, and is selected from the group consisting of HSSKLQ (SEQ ID NO:2), SS(Y/F)YS(G/S) (SEQ ID NO:3), Q/E)(R/K/H)RLXY (SEQ ID NO:4), PFT, KKSPGRVVGGSVAAH (SEQ ID NO:5), GPR, GPK, AP, RPPGFSPFR (SEQ ID NO:6), YEEEEI (SEQ ID NO:7), SNFDDY (SEQ ID NO:8), WMDF (SEQ ID NO:9), PLPL (SEQ ID NO:10), RR, FR, AND FR,

~~wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme, and the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases;~~

associating the polymer carrier with the first end of the ~~linker~~ enzyme cleavage site; and associating the drug molecule with the second end of the ~~linker~~ enzyme cleavage site,

and the polymeric carrier has a molecular weight of 50,000 or more or is greater than 6 nm in size.

13. (currently amended) A method of administering a drug to a patient, the method comprising steps of:

providing a patient having a disorder characterized by the overexpression of a ~~digestive~~ serine protease or matrix metalloproteinase enzyme;

administering to the patient a pharmaceutical composition that comprises a pharmaceutically acceptable excipient and an effective amount of a conjugate; and

~~administering the pharmaceutical composition to the patient;~~ wherein the conjugate comprises:

a polymeric carrier; a drug molecule; and ~~a linker~~ an enzyme cleavage site that is cleaved by a serine protease or matrix metalloproteinase that includes at least a first end and a second end, and is selected from the group consisting of HSSKLQ (SEQ ID NO:2), SS(Y/F)YS(G/S) (SEQ ID NO:3), Q/E)(R/K/H)RLXY (SEQ ID NO:4), PFT, KKSPGRVVGGSVAAH (SEQ ID NO:5), GPR, GPK, AP, RPPGFSPFR (SEQ ID NO:6), YEEEEI (SEQ ID NO:7), SNFDDY (SEQ ID NO:8), WMDF (SEQ ID NO:9), PLPL (SEQ ID NO:10), RR, FR, AND FR;

~~wherein the polymeric carrier conjugate is greater than about 6 nm in size,~~

wherein the polymeric carrier is associated with the first end of the ~~linker~~ enzyme cleavage site and the drug is associated with the second end of the ~~linker~~ enzyme cleavage site;

~~wherein the linker includes an oligopeptide recognition segment that is cleaved when the conjugate is exposed to the digestive enzyme; and~~

~~wherein the digestive enzyme is selected from the group consisting of serine proteases and matrix metalloproteinases~~

and the polymeric carrier has a molecular weight of 50,000 or more or is greater than 6 nm in size.

14. (previously presented) The conjugate of claim 1, wherein the polymeric carrier is dextran.

15. (currently amended) The conjugate of claim 1, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO:1).

16. (currently amended) The conjugate of claim 14, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO:1).

17. (previously presented) The conjugate of claim 1, wherein the drug is methotrexate.

18. (previously presented) The conjugate of claim 14, wherein the drug is methotrexate.

19. (previously presented) The conjugate of claim 15, wherein the drug is methotrexate.

20. (previously presented) The conjugate of claim 16, wherein the drug is methotrexate.

21. (previously presented) The conjugate of claim 1, wherein the drug is doxorubicin.

22. (previously presented) The conjugate of claim 14, wherein the drug is doxorubicin.

23. (currently amended) The conjugate of claim 22, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO:1).

24. (currently amended) The conjugate of claim 1, wherein the ~~digestive~~ enzyme is a serine protease.

25. (currently amended) The conjugate of claim 24, wherein the ~~digestive~~ enzyme is prostate specific antigen (PSA).

26. (currently amended) The conjugate of claim 24, wherein the ~~digestive~~ enzyme is human kallikrein 2 (hk2).

27. (currently amended) The conjugate of claim 24, wherein the ~~digestive~~ enzyme is urokinase-type plasminogen activator (uPA).

28. (currently amended) The conjugate of claim 24, wherein the ~~digestive~~ enzyme is fibroblast activating protein (FAP).

29. (currently amended) The conjugate of claim 1, wherein the ~~digestive~~ enzyme is a matrix metalloproteinase.

30. (currently amended) The conjugate of claim 29, wherein the ~~digestive~~ enzyme is Meprin.

31. (currently amended) The conjugate of claim 29, wherein the ~~digestive~~ enzyme is Meprin.

32. (currently amended) The conjugate of claim 29, wherein the ~~digestive~~ enzyme is MT1-MMP.

33. (currently amended) The conjugate of claim 29, wherein the ~~digestive~~ enzyme is matrix metalloproteinase II (MMP-2).

34. (currently amended) The method of claim 13, wherein the ~~digestive~~ enzyme is a serine protease.

35. (currently amended) The method of claim 34, wherein the ~~digestive~~ enzyme is prostate specific antigen (PSA).

36. (currently amended) The method of claim 34, wherein the ~~digestive~~ enzyme is human kallikrein 2 (hk2).

37. (currently amended) The method of claim 34, wherein the ~~digestive~~ enzyme is urokinase-type plasminogen activator (uPA).

38. (currently amended) The method of claim 34, wherein the ~~digestive~~ enzyme is fibroblast activating protein (FAP).

39. (currently amended) The method of claim 13, wherein the ~~digestive~~ enzyme is a matrix metalloproteinase.

40. (currently amended) The method of claim 39, wherein the ~~digestive~~ enzyme is Meprin.

41. (currently amended) The method of claim 39, wherein the ~~digestive~~ enzyme is Meprin.

42. (currently amended) The method of claim 39, wherein the ~~digestive~~ enzyme is MT1-MMP.

43. (currently amended) The method of claim 39, wherein the ~~digestive~~ enzyme is matrix metalloproteinase II (MMP-2).

44. (previously presented) The method of claim 13, wherein the polymeric carrier is dextran.

45. (currently amended) The method of claim 13, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO1:).

46. (currently amended) The method of claim 44, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO:1).

47. (previously presented) The method of claim 13, wherein the drug is methotrexate.

48. (previously presented) The method of claim 44, wherein the drug is methotrexate.

49. (previously presented) The method of claim 45, wherein the drug is methotrexate.

50. (previously presented) The method of claim 46, wherein the drug is methotrexate.

51. (previously presented) The method of claim 13, wherein the drug is doxorubicin.

52. (previously presented) The method of claim 44, wherein the drug is doxorubicin.

53. (previously presented) The method of claim 52, comprising ~~wherein the oligopeptide recognition segment comprise~~ the amino acid sequence IPVGLIG (SEQ ID NO:1) .

54-56. (cancelled)